Paper No. 32

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte RAMACHANDRAN S. RANGANATHAN,
RADHAKRISHNA PILLAI, PETER C. RATSEP,
RAJESH SHUKLA, MICHAEL F. TWEEDLE
and XUN ZHANG

Appeal No. 1999-1155
Application No. 08/241,253[1]

HEARD: June 14, 2001

Before WINTERS, SCHEINER and MILLS, Administrative Patent Judges.

SCHEINER, Administrative Patent Judge.

DECISION ON APPEAL

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[1] Application for patent filed May 11, 1994.

This is a decision on appeal under 35 U.S.C. § 134 from the examiner's final rejection of claims 1 through 12, 18 and 19. Claims 13 through 17 and 20 through 46, while still pending, have been withdrawn from consideration as directed to non-elected subject matter. Claims 1 and 5 are representative of the subject matter on appeal and are presented in Appendix B of the Examiner's Answer.[2]

The examiner relies on the following references:

Tweedle et al. (Tweedle)	4,885,363	Dec. 5, 1989
Parker et al. (Parker)	5,247,075	Sep. 21, 1993

PROCEDURAL MATTERS

In the first action (paper no. 7, December 26, 1995), claims 18 and 19 were "rejected for lack of unity of invention as being improper Markush claims of independent inventions;" claims 1 through 12 were rejected under 35 U.S.C. § 112, first and second paragraphs, as based on a non-enabling disclosure, and as indefinite; and claims 1 through 12, 18 and 19 were rejected under 35 U.S.C. § 103 as unpatentable over Tweedle and Parker. In the final rejection, the rejection of claims 1 through 12 under 35 U.S.C. § 112, second paragraph was withdrawn (paper no. 12, October 17, 1996).

Appellants submitted an amendment and declaration under 37 CFR § 1.132 in response to the final rejection (paper nos. 19 and 17 respectively, both dated April 21, 1997). The examiner withdrew the "Markush rejection" and the rejection under 35

[2] The claims presented in Appendix B correctly reflect entry of the amendment proposed in paper no. 19.

U.S.C. § 112, first paragraph, but maintained the rejection under 35 U.S.C. § 103, refusing to consider the declaration as "the elected invention is drawn to compounds; therefore the declaration emphasizing 'increased relaxi[v]ity' pertains to non-elected claims." (advisory action, paper no. 20, May 20, 1997). In addition, the examiner declined to enter the proposed amendment to the claims.

A second advisory action (paper no. 22, October 18, 1997) was issued in response to appellant's letter requesting reconsideration (paper no. 21, August 26, 1997). The second advisory action indicated that the previously proposed amendment to the claims would be entered upon the filing of an appeal. Meanwhile, appellants submitted their Brief on Appeal addressing the rejection of claims 1 through 12, 18 and 19 under 35 U.S.C. § 103 only (paper no. 24, October 20, 1997).

The rejection of claims 1 through 12, 18 and 19 under 35 U.S.C. § 103 as unpatentable over Parker and Tweedle was maintained in the Examiner's Answer (paper no. 25, January 16, 1998). In addition, an unspecified number of claims were newly rejected under the first and second paragraphs of 35 U.S.C. § 112, despite the examiner's assertion that the Examiner's Answer "does not contain any new ground of rejection" (paper no. 25, page 8, January 16, 1998). Appellants submitted a Reply Brief (March 19, 1998) addressing several points of argument raised for the first time in the Answer, as well as the two new rejections under the first and second paragraphs of 35 U.S.C. § 112, but the examiner made no response.

BACKGROUND

The present invention is directed to monomeric or multimeric metal-chelating compounds "having enhanced relaxivities."[3] The compounds are "useful in the form of metal complexes as diagnostic contrast agents," and "[w]hen the metal in the complex is paramagnetic, the diagnostic contrast agents are especially suitable for magnetic resonance imaging (MRI)." Specification, page 1. According to appellants, "[c]ontrast agents with significantly enhanced relaxivities are of great interest . . . because they offer improved efficiency at reduced doses for current clinical applications" and "also because they may provide the sensitivities needed for imaging various biochemical processes." Id., at page 11. "In one embodiment of the invention [e.g., claim 1], certain specific compounds comprise a tetraazacyclododecane macrocycle." Id., at page 1. In another embodiment, two or more tetraazacyclododecane monomers may be "linked by a cyclic bridging group" comprising "a 4- to an 8-membered carbocyclic ring." Id., at pages 7 and 8. In yet another embodiment of the invention (e.g., claim 5), the 4- to 8-membered carbocyclic ring links two or more monomers, wherein each monomer can be "any moiety capable of chelating a metal atom." Id., at page 8.

DISCUSSION

[3] According to the specification, "[t]he expression 'relaxivity' refers to the effectiveness of a metal chelate to reduce the relaxation time of bulk water in contact with the metal chelate," while "[t]he expression 'enhanced relaxivity' refers to relaxivity values made greater than those of well characterized prior art molecules by [] altering the electronic relaxation rate, T_s, through modifications of the of the metal-donor atom bond vibration frequencies and/or amplitudes, . . . in a multimer by decreasing the internal molecular motion of one monomer relative to another . . . or, [] by decreasing the molecular reorientation of a monomer or a multimer attached to a large moiety or physiological surface." Pages 3 and 4.

Obviousness

According to the examiner, Parker describes "tri-aza macrocycles, their metal complexes . . . and their conjugates with proteins and other molecules, . . . useful in diagnosis and therapy; and substituents CO_2H, SO_3H and PO_3H_2 among others," but "does not teach tetra-aza macrocycles." Tweedle, on the other hand, describes "tetra-aza macrocycles . . . , their metal complexes as Gd . . . ; use in imaging as contrast agents . . . ; use in radio therapy; and conjugating with biomolecules as antibodies." Examiner's Answer, pages 7 and 8.

With respect to those claims limited to monomeric or multimeric chelating compounds wherein the chelating moiety is a tetraazacyclododecane, e.g., claim 1, the examiner concludes that "[i]t would have been obvious, . . . in view of the commonality of properties and structure (macrocycles with 3 or more nitrogens) to substitute Parker's triaza macrocycle with Tweedle's tetra aza macrocycle, and obtain instant compounds," because

> (1) both are macrocycles with 3 or more nitrogens.
> (2) both complex with metals as Gd.
> (3) both are used in imaging; which is in turn dependent on 'relaxivities'.

Id., at page 8.

If we understand the examiner's rationale, it is that Parker's tri-azacyclo and Tweedle's tetra-azacyclo compounds are essentially interchangeable imaging agents because of their "commonality of properties and structure;" thus, it would have been obvious for one of ordinary skill in the art to have replaced the substituents on

Tweedle's core tetraazacyclododecanes with certain of the substituents from Parker's triazacyclononanes to arrive at the presently claimed tetraazacyclododecanes.

We do not agree. In our view, it is somewhat misleading to characterize the Parker and Tweedle references as describing "macrocycles with 3 or more nitrogens." Parker describes triazacyclononanes with three nitrogens, while Tweedle describes tetraazacyclododecanes with four. The two types of compounds are mutually exclusive, and thus, do not share "commonality of . . . structure." Moreover, the only "commonality of propert[y]" identified by the examiner is the ability of both tri-aza and tetra-azacyclo compounds to bind gadolinium (Gd). Finally, Parker describes metal complexes of tri-azacyclo compounds suitable for X-ray and radionuclide imaging, neither of which depends on relaxivity for effectiveness.

As set forth in In re Kotzab, 217 F.3d 1365, 1369-70, 55 USPQ2d 1313, 1316 (Fed. Cir. 2000):

> A critical step in analyzing the patentability of claims pursuant to section 103(a) is casting the mind back to the time of invention, to consider the thinking of one of ordinary skill in the art, guided only by the prior art references and the then-accepted wisdom in the field. [] Close adherence to this methodology is especially important in cases where the very ease with which the invention can be understood may prompt one "to fall victim to the insidious effect of a hindsight syndrome wherein that which only the invention taught is used against its teacher." []
>
> Most if not all inventions arise from a combination of old elements. [] Thus, every element of a claimed invention may often be found in the prior art. [] However, identification in the prior art of each individual part claimed is insufficient to defeat patentability of the whole claimed invention. [] Rather, to establish obviousness based on a combination of the elements disclosed in the prior art, there must be some motivation,

> suggestion or teaching of the desirability of making the specific combination that was made by the applicant. [citations omitted]

The examiner has established that certain of the elements of the claimed invention can be found in the prior art. Nevertheless, what is lacking from the examiner's treatment of the claims on appeal is a reason, suggestion or motivation, stemming from the prior art, which would have led a person having ordinary skill to the claimed method. Pro-Mold & Tool Co. v. Great Lakes Plastics, Inc., 75 F.3d 1568, 1573, 37 USPQ2d 1626, 1629 (Fed. Cir. 1996). In our judgment, the only reason or suggestion to modify the references to arrive at the present invention comes from appellants' specification.

Claims directed to multimeric chelating compounds wherein the chelating moiety can be "any moiety capable of chelating a metal atom," e.g., claim 5, are another matter entirely. Our determination of the patentability of these claims is hampered by the examiner's complete failure to acknowledge or address this embodiment of the invention in the statement of the rejection. 35 U.S.C. § 103 requires that obviousness be determined based on the claimed subject matter as a whole. Where, as here, the determination of obviousness is based on less than the entire claimed subject matter, the examiner's conclusion of obviousness is legally unsound and cannot stand.

On the record before us, we are constrained to reverse the examiner's rejection of claims 1 through 12, 18 and 19 under 35 U.S.C. § 103.[4]

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[4] Because we reverse on the basis of failure to establish a prima facie case of (continued...)

Enablement

In view of its brevity, we reproduce the examiner's rejection in its entirety:

> The terms 'optionally substituted', functional groups capable of forming a conjugate with a biomolecule are of such staggering breadth, the specification fails in meeting with the enablement (how to make) requirement i.e. how these plethora of diverse molecules are conjugated with the instant macromolecules. The long list of biomolecules on page 18, peptides, polypeptides, oligosaccharides . . . fragments of RNA, DNA are too diverse chemically and too functional legally.

It is well settled that the examiner bears the initial burden of providing reasons why a supporting disclosure does not enable a claim. In re Marzocchi, 439 F.2d 220, 223, 169 USPQ 367, 369 (CCPA 1971). While the claims are indeed broad, we agree with appellants that the examiner has not provided a reasonable basis to question whether the specification would enable one skilled in the art to make the claimed compounds, particularly in light of Dr. Ranganathan's assertion that "[t]he conjugation of the groups . . . in [the] claims . . . with a biomolecule of the claims is a process well known in the art" and "a matter of routine."[5] Accordingly, the rejection is reversed.

Indefiniteness

Again, in view of its brevity, we reproduce the examiner's rejection:

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[4](...continued)
obviousness, we find it unnecessary to comment on the declaration submitted April 21, 1997 under 37 CFR § 1.132 as it pertains to unexpected properties of the claimed compounds. In re Geiger, 815 F.2d 686, 688, 2 USPQ2d 1276, 1278 (Fed. Cir. 1987).

[5] See paragraph 13 of the declaration submitted under the provisions of 37 CFR § 1.132 (paper no. 17, April 21, 1997).

> The instant inventions fail to distinctly claim the invention because one does not know a) specific substituents (optionally) substituted b) specific functional groups c) specific biomolecule and d) specific multimer.
>
> The terms a) "including" in amended claim 1, including monoclonal antibodies b) fragments thereof are rejected under 35 USC 112, second paragraph for lack of clear claiming. The use of the 'including', leaves the claim language open; one to ask what else is included? Similarly, 'fragments thereof' is unclear. The cited terms in claim 1 is not a proper claim structure in this country.

To the extent that the examiner is concerned that the claims are broad, we remind the examiner that, in and of itself, "[b]readth is not indefiniteness," In re Gardner, 427 F.2d 786, 788, 166 USPQ 138, 140 (CCPA 1970). We agree with appellants that "[a] person of skill in the art could read [a]ppellants' claims and determine whether a given claim fell within them." Reply Brief, page 5. The rejection is reversed.

OTHER ISSUES

The Search

As discussed above, claim 1 is drawn to a monomeric or multimeric chelating agent, wherein the chelating agent is a tetraazacyclododecane. Independent claim 5, also drawn to a chelating agent, is narrower than claim 1 in the sense that it requires two or more chelating moieties linked through a 4- to 8-membered carbocyclic ring; on the other hand, claim 5 is broader than claim 1 in that no particular chelating moiety is specified. The administrative file of this application indicates that a computer data base

search was performed for prior art relating to tetraazacyclododecanes, and that subclasses 465 and 474 of Class 540, pertaining to particular heterocyclic compounds, including tetraazacyclododecanes, were searched. However, there is nothing to indicate that the embodiment of the claimed invention represented by claim 5 was ever searched by the examiner. Upon return of the application to the group, the examiner should review the record and ensure that a complete and proper search of the subject matter claimed has been conducted.

Indefiniteness

The examiner's rejections of unspecified claims under the first and second paragraphs of 35 U.S.C. § 112 can only be described as perfunctory in nature, and we have reversed the rejections as lacking underlying factual support or analysis. Nevertheless, the phrase "each R' is independently hydrogen or alkyl, alkoxy, cycloalkyl, hydroxyalkyl or aryl, each of which is optionally substituted" (in claim 1, e.g.), appears to be incomplete in the absence of an indication of appropriate substituting moieties. Upon return of the application to the examining group, appellants and the examiner should determine whether the claim is indeed incomplete when read in light of the specification.

CONCLUSION

For the reasons set forth in the body of this opinion, we reverse the rejection of claims 1 through 12, 18 and 19 under 35 U.S.C. § 103, as well as the rejections of the claims under the first and second paragraphs of 35 U.S.C. § 112. In addition, we raise two issues for the examiner's consideration upon return of the application.

REVERSED

Sherman D. Winters Administrative Patent Judge	)
Toni R. Scheiner Administrative Patent Judge	) BOARD OF PATENT) APPEALS AND) INTERFERENCES
Demetra J. Mills Administrative Patent Judge	)

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